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Description

Field of the Invention

This invention relates to tablets containing means to mask the taste of active ingredients and/or provide sustained release of such ingredients. More particularly, the means of providing taste masking and/or sustained release of active ingredients are coatings comprising blends of hydroxypropyl cellulose with cellulose acetate and/or cellulose acetate butyrate.

BACKGROUND OF THE INVENTION

Orally administered medicaments are given to the patient in many forms, such as liquid solutions, emulsions, or suspensions, or in solid form such as capsules or tablets (as used herein, the term "tablet" means any shaped and compressed solid dosage form, including caplets). Medicaments administered in tablet or capsule form are usually intended to be swallowed whole. Therefore, the often disagreeable taste of the active ingredient need not be taken into account in formulating the medicine, except for the provision of means to prevent the taste from being apparent during the short time that the medicine is in the mouth. Such means may include the provision of an appropriately thin and quickly dissolving coating on the tablet, the use of the gelatin capsule form (the gelatin outer shell of the capsule keeps the active ingredient inside until the capsule has been swallowed), or simply compressing a tablet firmly so that it will not begin to disintegrate during the short time that it is intended to be in the mouth.

Children, older persons, and many other persons have trouble swallowing whole tablets and even capsules. Therefore, in cases where the dosage to be administered cannot be made into a very small tablet or capsule, it is desirable to provide the medicine either in liquid form or in a chewable solid form, in addition to the tablet or capsule that is designed to be swallowed whole. Even where the medicine can be formulated as a liquid, it is desirable also to be able to provide a chewable solid form because it is usually more convenient to carry a supply of tablets with oneself all day than a container of liquid medicine.

A common problem with chewable tablet forms is the often disagreeable taste of the active ingredient which manifests itself during chewing. In some cases, the taste of the active medicament in a tablet can be overpowered by adding flavoring ingredients to the tablet so that when it is chewed the taste of the active ingredient is simply overpowered. For instance, this has been done with children's aspirin where the dosage is small enough so that the amount of flavoring agents needed to mask the taste of the medicine is not so great that the tablet becomes unreasonably large. A children's size tablet of acetaminophen (acetyl para-aminophenol or "APAP") is available commercially wherein the APAP is present in granules that are coated with ethyl cellulose. A significant proportion of the APAP remains shielded by the coating (and therefore does not contribute to taste) while the tablet is in the mouth, despite some breakage of the ethyl cellulose coating during compression of the tablet and some additional breakage of the coating during chewing. The APAP becomes bioavailable via permeation through the coating (although ethyl cellulose is not soluble in aqueous fluids, water does permeate through the coating) and from the granules wherein the coating was broken.

GB-A-2166651 describes a controlled release powder and processes for its preparation. The powder comprises microparticles with an average size in the range 0.1 to 125 µm, each of the microparticles being in the form of a micromatrix of an active ingredient uniformly distributed in at least one non-toxic polymer. Suitable non-toxic polymers include cellulose acetate (CA), cellulose acetate butyrate (CAB), polyvinylpyrrolidene (PVP) and hydroxypropyl cellulose (HPC).

EP-A-0317274 discloses chewable medicament tablets wherein the granules of active ingredient are coated with a blend of cellulose acetate or cellulose acetate butyrate and polyvinylpyrrolidene (PVP) in order to mask the disagreeable taste of the active ingredient.

The present invention is directed to the discovery of a coating that can be used to coat granules of active medicament and which can achieve a better balance between taste masking and control of bioavailability than can be achieved with ethyl cellulose or other previously known combinations. Further, the coating of the invention can provide a sustained release coating for medicaments.

As embodied and fully described herein the present invention provides a chewable tablet of a medicament comprising compressed coated granules, said coated granules individually comprising medicament coated with from 5% to 28% by weight, based on the dry weight of the coated medicament granules, of a polymer blend of: (a) cellulose acetate (CA), cellulose acetate butyrate (CAB) or a combination thereof; and (b) hydroxypropyl cellulose (HPC), wherein the weight ration of (a):(b) is in the range of 97:3 to 50:50. The coating provides excellent taste masking while still permitting acceptable bioavailability of the active

ingredient. Further, the coating can provide for sustained release of the medicament. The coated medicament is included in a chewable tablet comprising compressed individual particles of medicament particles coated with a blend of CA and/or CAB and HPC.

In further preferred embodiments, ibuprofen particles are coated with a blend of CA and/or CAB and HPC and are then compressed into tablet form together with flavoring agents and other ingredients that are customarily used in making such chewable tablets.

The invention also provides a process of making and methods using the chewable tablets, as well as, a method of using the coated medicament particles for sustained release of the active ingredients.

DETAILED DESCRIPTION OF THE INVENTION

The invention will now be described specifically in terms of its most preferred embodiments which is the preparation of chewable tablets of ibuprofen, a medicament used in both over-the-counter preparations and in prescription drugs for analgesic and antipyretic purposes. Reference will also be made in detail herein to other preferred embodiments of the compositions, processes and methods of the invention.

In the preferred embodiment of the process of the invention, medicament, preferably ibuprofen in granular form, is coated with a blend of HPC and CA and/or CAB so that the granules are coated with the polymer blend. The coated granules, together with other ingredients such as flavoring agents, extenders, exipients, and the like, are compressed into tablet form. (As used herein, the term "granule" refers to individual particles or to agglomerates of individual particles of the medicament.) A high enough proportion of the coating remains effectively intact on the ibuprofen granules through the compression of the tablet and through normal chewing in the mouth to permit effective taste masking of the normally bitter tasting ibuprofen. The term "effectively intact" means that the coating remains sufficiently integral to mask the taste or flavor of the medicament detectable through the coating. This taste masking provides a mean to limit the quantity of other flavoring agents in the tablet is not be so large that an excessively large tablet is required to overpower rather than mask the unpleasant flavor of the medicament.

When the coated granules are swallowed, the active medicament becomes bioavailable via permeation through the coating. Permeation can occur through the intact coating as well as through the coating that has become porous through dissolution of the water soluble HPC component of the coating; the CA and CAB components are water insoluble. Permeation also occurs via disintegration of the coating, which is caused in part by chewing, in part by processing of the tablet (compression), and in part by removal of the HPC component of the coating by dissolution.

The coating may be designed so that the medicament is released relatively rapidly or in a sustained release mode, depending on the proportion of coating to medicament in the granules, or the proportion of the CA and/or CAB to HPC in the coating, or their combination. Generally, higher proportions of HPC used in the coating leads to more rapid release of the medicament.

Cellulose acetate and cellulose acetate butyrate are quite water insoluble but are soluble in organic solvents. They can provide good taste masking properties since they do not dissolve in the mouth and are tough enough to remain effectively intact during processing and normal chewing in the mouth. If used alone, however, a coating of CA and/or CAB would not provide adequate bioavailability of the active ingredient after swallowing the chewed tablet. To provide the requisite bioavailability, HPC is added. HPC is a polymer which is soluble in both water and organic solvents. The water solubility of HPC provides the bioavailability of the active medicament in the GI tract via the mechanisms discussed above. The solubility of HPC in organic solvents permits ready mixing with CA or CAB during the production of the coated granules, since CA and CAB are not very soluble, if at all, in water, and are most conveniently applied from an organic solvent solution. HPC and CA and/or CAB form clear compatible solutions in organic solvents, preferably acetone/methanol mixtures, which are suitable for pharmaceutical coating. The blend of CA and/or CAB and HPC provides the balance needed for good taste masking while being chewed in the mouth, along with either rapid or sustained bioavailability of the active medicament in the GI tract after swallowing.

The HPC and CA and/or CAB blends of the invention have been found to be more versatile than the PVP blends of Julian and Radebaugh discussed earlier. Due to the superior flexibility of HPC polymer as compared to PVP, higher percentages of HPC (up to 50%) can be used than is recommended by Julian and Radebaugh for PVP (3 to 30%). Higher amounts of the water soluble component HPC increases the rate and extent of disintegration of the coating thus increasing the porosity of the coating. Presence of such higher amount of the water soluble component HPC advantageously increases the bioavailability of the coated medicaments.

The coating used is a blend containing 50 to 97 percent of CA and/or CAB, by weight of the coating, and 3 to 50 percent HPC. Within the range indicated, if sustained release of the medicament is desired, a lower proportion of the water soluble HPC may be used. When rapid release of the medicament is desired a higher proportion of the water soluble HPC is used, i.e. up to 50 percent. Routine experimentation will suffice to determine the appropriate proportions of the two polymers to use in individual cases, as is more specifically illustrated below. The upper limit of 50 percent HPC is limited by practical processing considerations. The tackiness of the coating solution increases in the higher range amounts of HPC and amounts over 50 percent may lead to particle agglomeration during the coating process. Further, the rate of release can be controlled by use of HPC of specific molecular weight, whereby, higher molecular weight HPC leads to a slower release of medicament.

The coated granules may be made by coating the granules of medicament with an organic solvent solution of the polymers in a fluidized bed coating operation. A wide variety of organic solvents may be used to prepare the organic solvent solution of the coating polymers. For instance, a preferred solvent is acetone-methanol, but other solvent systems may also be used, including methylene chloride-methanol (e.g. 9:1), acetone-ethyl acetate, toluene-ethanol, and others. As a general rule, the proportion of polymer in the solvent solution will be from 5 to 20 and preferably 8 to 15 weight percent for optimal taste masking and rapid release of drug depending upon the specific solvents used and other similar considerations.

The polymers are dissolved in the solvent and the polymer solution is then coated onto ibuprofen or other medicament active ingredient or combination of ingredients granules, using a fluidized bed coater. Air (which may be heated) passes through a bed of the medicament granules to fluidize them, and the solvent solution of the two polymers is sprayed onto the fluidized bed and thereby coats the granules. The air passing through the bed dries the coated granules, so that a dry coated granule is obtained. The coated granules are then used in combination with various excipients, flavors, and colors to make a chewable tablet.

The dried coating as thus applied usually constitutes 5-20%, more preferably 8-15% of the total dry weight of the coated ibuprofen granule. The exact proportions of coating to medicament desired for individual cases can be determined by routine experimentation. The amount of coating may be varied in light of the intended application and desired bulk of the products. Chewable tablets can be acceptable in larger sizes than swallowed tablets since chewing will reduce the size of the tablets in the mouth. Further, tablets intended for pediatric use generally comprise reduced dosage amounts and less bulk. Larger proportions of coating may be used to provide a sustained release or better taste formulation.

When two or more medicaments are utilized in a tablet the coatings may be varied to provide a slower release of one medicament over another. This is especially advantageous for dosing a combination of medicaments that are more effectively released in different parts of the digestive tract or are better released separately in the digestive tract to avoid interference with each other or other incompatibility. Further, the same medicament may be subject to different coating composition and amounts to provide for sustained release of some portion of the medicament and immediate release of another portion of the medicament to achieve an optimal dosing versus time profile. Obtaining such optimal dosing/time profiles depends upon the particular medicaments and medical needs required. The exact proportions of coating materials used to achieve these profiles can be determined by routine experimentation.

While exact size of the coated granules has not been found to be critical, the coated granules will usually be sized to pass between between a 10 and 200 mesh sieve screen (U. S. Sieve Series). In the usual case, the coated granules will be sized from 40 to 60 mesh.

In addition to ibuprofen, any solid medication in need of taste masking can be used in the invention. Illustrative examples include aspirin, naproxen, acetaminophen, pseudoephedrine, substantially pure dexibuprofen (i.e. less than 20% of the inactive R-antipode), dexibuprofen lysine, cimetidine, ranitidine, nizatidine, psuedoephedrine hydrochloride, chlorpheniramine maleate, dextromethorphan hydrobromide, diphenhydramine hydrochloride or citrate, dextromethorphan, chlorpheniramine, loperimide, simethicone, salts thereof and combinations thereof. Identification of medicaments herein is intended to apply to pharmaceutically acceptable salts thereof as well. Further, the coating of the invention provides a convenient means for providing sustained release of medicaments and for presenting a viable dosage form for combination medicaments which are incompatible before (during storage) or after administration or for medicaments which are desirably released in the GI tract at various times or in various places thereof.

Examples

The following procedure and Examples provide examples of preferred method and materials for practicing the present invention. These Examples should be considered illustrative only.

An illustrative preferred procedure for preparing the coated granules of medicament in accordance with the invention is the following:

A solution of the coating polymers is prepared in an organic solvent by simply adding the polymers to the solvent with stirring. The medicament, in granular form, is placed in a fluidized bed coater and is fluidized by a flow of warm air. The temperature of the air has not been found to be narrowly critical, and can vary over a wide range, keeping in mind the fact that the temperature should not be high enough to cause decomposition, sintering, or melting of the medicament granules. When coating ibuprofen granules, a temperature of from 55° to 75°C is suitable but such temperature ranges will change depending on the medicament being coated. The rate of air flow is adjusted so as to fluidize the granules. Such flow will vary depending on factors such as the specific equipment used, the size of the charge of granules, the size of the individual granules, the apparent specific gravity of the granules, and other factors that are known to the worker in the arts relating to fluidized bed coating.

After the medicament has been fluidized, the polymer solution is sprayed on top of the fluidized bed. The air flow through the bed is continued until the amount of solvent remaining in the coating has been reduced to parts per million levels. The granules are actually dry to the touch within a very short time after the coating solution has been sprayed onto the granules of medicament; a matter of a few seconds in some cases. However, the total drying time required to ensure that the organic solvent content of the coating has been reduced to the level desired may take much longer, depending on the temperature of the air, the size of the batch, and the like. For batches of ibuprofen weighing four to six kilograms, total drying times of the order of one to three hours have been used. Routine experimentation will suffice to determine the appropriate air temperatures and total times required in the fluidized bed coaters in individual cases.

The Examples below set forth the ingredients and proportions for typical laboratory scale preparations of coated medicament granules. The materials used are the following:

Ibuprofen - In the form of granules having a particle size of about 60 mesh;

Loperamide (HCl salt) - In the form of granules having a particle size of 40-80 mesh;

APAP - Acetaminophen USP granules having a particle size of 170-270 μm;

Famotidine - In the form of granules having a particle size of 170-270 μm;

Dexibuprofen lysine - substantially pure granules of S-ibuprofen lysine salt with less than 20 and preferably less than 10% of the inactive R-ibuprofen antipode present.

CA - Cellulose acetate NF powder, for example, CA 398-10 or CA-320S available from the Food and Pharmaceutical Products Division of FMC may be used. The CA 398-10 polymer has an acetyl content of about 39.8%, by weight, a hydroxyl content of 3.4%, by weight, a degree of substitution of 2.7, and a solution viscosity of about 38 poises or 10 seconds, determined by ASTM Method D 1343 in the solution described as Formula A, ASTM Method D 871. According to the manufacturer, the typical weight average molecular weight is 177,000 and the typical number average molecular weight is 58,500. The CA-320-S polymer has an acetyl content of about 32.0%, by weight, a hydroxyl content of about 9.0%, by weight, and a degree of substitution of 2.1. The manufacturer reports a solution viscosity in 90:10 CH_2Cl_2:methanol, at 4% (w/w) concentration, of 50 cps. Typical weight average molecular weight is 100,500 and typical number average molecular weight is 63,500, according to the manufacturer. (Viscosities in poises are converted to ASTM seconds equivalent to values obtained under ASTM Method D 871.);

CAT - Cellulose triacetate powder, CA-435-75S is also available from FMC. This CAT's acetyl content is 43.5 and the solution viscosity is 68 seconds, determined by the "Ball Drop Method" of ASTM D 1343, using the solution designated "Formula D" in Table 2 of ASTM D 871;

CAB - Cellulose acetate butyrate, CAB 171-15S from FMC. The polymer has a butyryl content of 17 weight percent, an acetyl content of 29.5 weight percent, and a viscosity of 24 cps in a 4 weight percent solution in methylene chloride:methanol (90:10) one day after solution preparation. The viscosity is taken at about 25°C;

HPC - Hydroxypropyl cellulose having a molecular weight of 80,000 to 370,000. Suitable HPC includes those available from Aqualon in the grades known by the tradenames KLUCEL® EF, LF, JF or GF.

The term "total coat" refers to the proportion of coating to medicament in the coated granule product, "charge" to the weight of medicament, "polymer solution" to the proportion of polymer in the organic solvent solution, and "total batch" to the weight of medicament plus coating.

Examples I-X, below, display the identity of medicament(s), coating polymers, organic solvents and organic solvent solutions of coating polymers, and the proportions of all of these materials for typical laboratory scale batches of coated medicament granules for use in the invention in accordance with the preferred procedure for preparing coated granules of medicament as described above.

Example I

Active -	Acetaminophen
Form of Active -	Granular APAP with particle size of 170 - 270 µm.
Coating Solution -	Cellulose Acetate 398-10/ Klucel LF in Acetone/Methanol 80/20 at 8-12% solids.
Note:	Klucel LF has a weight average molecular weight of 95,000. Klucel EF (Molecular Weight 80,000) can also be used.
Blend Ratio	70/30 to 90/10 (CA/HPC) for taste masking. 85/15 to 97/3 for sustained release.
Coat Level	10-15% for taste masking. 16-28% for sustained release.

Example II

Active -	Acetaminophen
Form of Active -	Rotogranulated APAP with smooth, approximately spherical shape. Size of 170 - 270 µm.

Otherwise same as above for I.

Example III

Active -	Famotidine
Form of Active -	Rotogranulated with a carrier such as lactose which results in a smooth, approximately spherical shape. Binders such as povidone can be included in the Rotogranulated particles at levels of 1-10%. Same granular size as in I.
Coat Level	7-15% for taste masking.

Otherwise same as above for I.

Example IV

Active -	Dexibuprofen lysine (or other salts of ibuprofen such as Sodium Ibuprofen)
Form of Active -	Rotogranulated particles can include a binder such as Povidone at levels of 1 - 10%. Granular size of 170 - 270 µm.
Coat Level:	10 - 18% for taste masking.

Example V

Active -	Naproxen Sodium
Form of Active -	Rotogranulated as in Example IV.

Otherwise same as above for IV.

Example VI

Total Coat	12 % w/w		
Charge 4000 gms		ibuprofen	
Total Polymer			545.45 gms
Polymer 1	65 % w/w	CA	354.54 gms
Polymer 2	10 % w/w	CAB	54.55 gms
Polymer 3	25% w/w	HPC	136.36 gms
Polymer Soln	10 % w/w		5454.55 gms
Solvent 1	80 % w/w	acetone	3927.27 gms
Solvent 2	20 % w/w	methanol	981.82 gms
	Total Batch		4545.45 gms

Example VII

Total Coat	12 % w/w		
Charge 4000 gms		ibuprofen	
480 gms		pseudoephedrine	
Total Polymer			545.45 gms
Polymer 1	60 % w/w	CA	327.27 gms
Polymer 2	40 % w/w	HPC	218.18 gms
Polymer Soln	8 % w/w		6818.18 gms
Solvent 1	80 % w/w	acetone	5018.18 gms
Solvent 2	20 % w/w	methanol	1254.55 gms
	Total Batch		5025.45 gms

Example VIII

Total Coat	12 % w/w			
Charge	4000 gms		APAP	
	480 gms		pseudoephedrine	
	32 gms		chlorpheniramine	
	240 gms		dextromethorphan	
Total Polymer				545.45 gms
Polymer 1	70 % w/w		CA	381.82 gms
Polymer 2	30 % w/w		HPC	163.63 gms
Polymer Soln	10 % w/w			5454.55 gms
Solvent 1	80 % w/w		acetone	3927.27 gms
Solvent 2	20 % w/w		methanol	981.82 gms
		Total Batch		5297.45 gms

Example IX

Total Coat	12 % w/w			
Charge	4000 gms		aspirin	
Total Polymer				545.45 gms
Polymer 1	85 % w/w		CA	463.64 gms
Polymer 2	15 % w/w		HPC	81.82 gms
Polymer Soln	8 % w/w			6818.18 gms
Solvent 1	90 % w/w		acetone	5645.45 gms
Solvent 2	10 % w/w		ethyl acetate	627.27 gms
		Total Batch		4545.45 gms

Example X

Total Coat	12 % w/w		
Charge 4000 gms		loperamide HCl	
Total Polymer			545.45 gms
Polymer 1	80 % w/w	CA	436.36 gms
Polymer 2	20 % w/w	HPC	109.09 gms
Polymer Soln	8 % w/w		6818.18 gms
Solvent 1	80 % w/w	acetone	5018.18 gms
Solvent 2	20 % w/w	methanol	1254.55 gms
	Total Batch	4545.45 gms	

Example XI

Total Coat	12 % w/w		
Charge 4000 gms		APAP	
Total Polymer			545.45 gms
Polymer 1	85 % w/w	CAB	463.64 gms
Polymer 2	15 % w/w	HPC	81.82 gms
Polymer Soln	8 % w/w		6818.18 gms
Solvent 1	80 % w/w	CH_2Cl_2	5018.18 gms
Solvent 2	20 % w/w	methanol	1254.55 gms
	Total Batch		4545.45 gms

Example XII

Various other medicament combinations are prepared by coating desirable dosage ranges of medicaments cimetidine, ranitidine and nizatidine and combinations of two or more of pseudeuphedrine HCl, chlorpheniramine maleate, dextromethorphan HBr, diphenhydramine HCl or citrate, acetaminophen, ibuprofen and naproxen in accordance with the procedure and coatings of any of Examples I-XI

While the use of fluidized bed coating has been described in some detail as one preferred method for making the coated granules that are utilized in the invention, other techniques for making the coated granules may be used. Such other techniques include various microencapsulation techniques such as coacervation and solvent evaporation.

The following examples XI-XIV describes preparation of chewable tablets.

Example XIII

The ingredients displayed below, are sieved, dry blended, and compressed by standard procedures into round (disc shaped) chewable tablets, each weighing 1100 milligrams. The tablets had diameters of 1.43cm (9/16 inch), thicknesses of 0.573 centimeter, and had volumes of 0.919 cubic centimeter. Each tablet contained 200 milligrams of active ibuprofen per tablet, from coated granules prepared in accordance with the procedure of Example 1 containing 15 weight percent coating in which the proportion of CA:HPC was 85:15% w/w. The table below displays the ingredients, mg/tablet, percent, and grams/batch sufficient to make 10,000 tablets.

Component	mg/Tablet	Percent	Gms/Batch
mannitol	611.79	64.75	6117.94
AVICEL® PH101	71.76	7.59	717.65
aspartame	11.84	1.25	118.41
citric acid (anhyd)	5.74	0.61	57.41
flavor	4.31	0.46	43.06
PROSWEET®	2.87	0.30	28.71
Mg stearate	9.33	0.98	93.29
coated ibuprofen	227.27	24.05	2272.70

The following table displays some typical proportion ranges for the ingredients that were used in Examples XIII:

TABLE

Component	Range of Proportions, %
mannitol	30 - 70
AVICEL® PH101	5 - 12
aspartame	0.5 - 3
citric acid	0.1 - 2
flavor	0.2 - 2
PROSWEET®	0.1 - 2
mg stearate	0.4 - 2
coated ibuprofen	10 - 50

The functions of the several ingredients and some typical replacements for them are as follows:
Mannitol is a sweetener. It can be replaced by dextrose, fructose, sorbitol, compressible sugar, or lactose;
Avicel® PH101 is microcrystalline cellulose. It is used as a tabletting aid, e.g. to impart hardness. It may be replaced with tricalcium phosphate;
Aspartame is an artificial sweeetener. It can be replaced with others such as saccharin;
Citric acid is used as an acidifying agent to enhance the taste. It can be replaced by other acidifying agents such as malic acid;
The flavoring agent can be any flavoring agents such as vanilla, peppermint, orange, cherry, or spearmint;
Prosweet® is another sweetener. It can be replaced with other materials such as saccharin, aspartame, natural sugars; and
Magnesium stearate is a lubricant (to lubricate the dye walls and punches used during the tablet compression procedure). It can be replaced by talc, stearic acid, calcium stearate, zinc stearate, or the like.

For example, other components may be added to the tablets including additional actives, various flavorings, preservatives and other pharmaceutical excipients. The present invention may also be used to provide a sustained release and/or chewable form for vitamins, minerals or other nutrients.

Application of the compositions and processes of the present invention for medical and pharmaceutical uses can be accomplished by any clinical, medical and pharmaceutical methods and techniques as are presently and prospectively known to those skilled in the art.

Claims

1. A chewable tablet of a medicament comprising compressed coated granules, said coated granules individually comprising medicament coated with from 5 to 28% by weight, based on the dry weight of the coated medicament granule, of a polymer blend of: (a) cellulose acetate, cellulose acetate butyrate or combinations thereof, and (b) hydroxypropyl cellulose, wherein the weight ratio of (a): (b) is from 97:3 to 50:50.

2. A chewable tablet according to claim 1, wherein the medicament is selected from the group consisting of ibuprofen, dexibuprofen lysine, acetaminophen, aspirin, naproxen, pseudoephedrine, dextromethorphan, chlorpheniramine, loperamide, diphenhydramine, famotidine, cimetidine, ranitidine, nizatidine,

salts thereof, and combinations thereof.

3. A chewable table according to claim 1 or 2, wherein the coated granules contain from 5 to 20% by weight, based on the dry weight of the coated medicament granules, of the said polymer blend.

4. A chewable tablet according to claim 3, wherein the coated granules contain from 8 to 15% by weight, based on the dry weight of the coated granules, of the said polymer blend.

5. A chewable tablet according to any preceding claim, wherein the medicament is selected from the group consisting of: (a) ibuprofen; (b) dexibuprofen lysine; (c) a combination of ibuprofen and pseudoephedrine; (d) loperamide; (e) acetaminophen and diphenhydramine hydrochloride or citrate; (f) a combination of acetaminophen, pseudoephedrine, dextromethorphan and chlorpheniramine; or (g) a combination of an analgesic selected from the group consisting of ibuprofen, acetaminophen and aspirin with pseudoephedrine, chlorpheniramine or dextromethorphan.

6. A process to prepare a chewable medicament table comprising the steps of:
coating medicament granules with from 5 to 28% by weight, based on the dry weight of the coated medicament granules, of a polymer blend of: (a) cellulose acetate, cellulose acetate butyrate or a combination thereof, and (b) hydroxypropyl cellulose, wherein the weight ratio of (a):(b) is from 97:3 to 50:50; and
forming a chewable tablet by compressing the coated medicament in the presence of excipients.

7. A method according to claim 6, wherein the medicament comprises ibuprofen, aspirin, naproxen, acetaminophen, loperamide, pseudoephedrine, dextromethorphan, chlorpheniramine, diphenydramine, famotidine, cimetidine, ranitidine, nizatidine, or salts or mixtures thereof.

8. A method according to claim 6, wherein the medicament is dexibuprofen lysine.

Patentansprüche

1. Eine kaubare Tablette eines Medikamentes umfassend komprimierte überzogene Körnchen, wobei besagte überzogene Körnchen individuell ein Medikament umfassen, mit einem Ueberzug von 5 bis 28 Gewichtsprozent, basierend auf dem Trockengewicht des überzogenen Medikamentenkörnchen, eines Polymerenblends aus: (a) Celluloseacetat, Celluloseacetatbutyrat oder Kombinationen davon, und (b) Hydroxypropylcellulose, wobei das Gewichtsverhältnis von (a) : (b) gleich 97:3 bis 50:50 ist.

2. Eine kaubare Tablette gemäß Anspruch 1, wobei das Medikament aus der Gruppe bestehend aus Ibuprofen, Dexibuprofen, Lysin, Acetaminophen, Aspirin, Naproxen, Pseudoephedrin, Dextromethorphan, Chlorpheniramin, Loperamid, Diphenhydramin, Famotidin, Cimetidin, Ranitidin, Nizatidin, Salze derselben und Kombinationen daraus, ausgewählt ist.

3. Eine kaubare Tablette gemäß Anspruch 1 oder 2, wobei die überzogenen Körnchen zwischen 5 bis 20 Gewichtsprozent, basierend auf dem Trockengewicht der überzogenen Medikamentenkörnchen, des besagten Polymerenblends enthalten.

4. Eine kaubare Tablette gemäß Anspruch 3, wobei die überzogenen Körnchen 8 bis 15 Gewichtsprozent, basierend auf dem Trockengewicht der überzogenen Körnchen, des besagten Polymerenblends enthalten.

5. Eine kaubare Tablette gemäß irgendeinem der vorherigen Ansprüche, wobei das Medikament ausgewählt ist aus der Gruppe bestehend aus: (a) Ibuprofen; (b) Dexibuprofen Lysin; (c) einer Kombination aus Ibuprofen und Pseudoephedrin; (d) Loperamid; (e) Acetaminophen und Diphenhydramin-Hydrochlorid oder -Citrat; (f) einer Kombination von Acetaminophen, Pseudoephedrin, Dextromethorphan und Chlorpheniramin; oder (g) einer Kombination eines Analgetikums ausgewählt aus der Gruppe bestehend aus Ibuprofen, Acetaminophen und Aspirin mit Pseudoephedrin, Chlorpheniramin oder Dextrometorphan.

6. Ein Verfahren zur Herstellung einer kaubaren Medikamententablette umfassend die Schritte:

Ueberziehen von Medikamentenkörnchen mit einem Ueberzug von 5 bis 28 Gewichtsprozent, basierend auf dem Trockengewicht der überzogenen Medikamentenkörnchen, eines Polymerenblends aus: (a) Celluloseacetat, Celluloseacetatbutyrat oder einer Kombination davon, und (b) Hydroxypropylcellulose, wobei das Gewichtsverhältnis von (a) : (b) gleich 97:3 bis 50:50 ist; und

Bilden einer kaubaren Tablette durch Komprimieren des überzogenen Medikamentes in Anwesenheit von Füllstoffen.

7. Ein Verfahren gemäß Anspruch 6, wobei das Medikament Ibuprofen, Aspirin, Naproxen, Acetaminophen, Loperamid, Pseudoephedrin, Dextromethorphan, Chlorpheniramin, Diphenhydramin, Famotidin, Cimetidin, Ranitidin, Nizatidin, Salze oder Kombinationen derselben umfasst.

8. Ein Verfahren gemäß Anspruch 6, wobei das Medikament Dexibuprofen Lysin ist.

Revendications

1. Un comprimé à mâcher d'un médicament comprenant des granulés enrobés comprimés, lesdits granulés enrobés comprenant chacun un médicament enrobé avec 5 à 28 % en masse, sur la base de la masse sèche du granulé de médicament enrobé, d'un mélange polymère: (a) d'acétate de cellulose, d'acétobutyrate de cellulose ou de combinaisons de ceux-ci, et (b) d'hydroxypropylcellulose, dans lequel le rapport de masse entre (a) et (b) est compris entre 97:3 et 50:50.

2. Un comprimé à mâcher selon la Revendication 1, dans lequel le médicament est sélectionné parmi le groupe composé d'ibuprofène, de lysine de dexibuprofène, d'acétaminophène, d'aspirine, de naproxène, de pseudoéphédrine, de dextrométhorphan, de chlorphéniramine, de lopéramide, de diphénhydramine, de famotidine, de cimétidine, de ranitidine, de nizatidine, de sels et de combinaisons de ceux-ci.

3. Un comprimé à mâcher selon la Revendication 1 ou 2, dans lequel les granulés enrobés contiennent 5 à 20 % en masse, sur la base de la masse sèche des granulés de médicament enrobés, dudit mélange polymère.

4. Un comprimé à mâcher selon la Revendication 3, dans lequel les granulés de médicament contiennent 8 à 15 % en masse, sur la base de la masse sèche des granulés enrobés, dudit mélange polymère.

5. Un comprimé à mâcher selon l'une quelconque des Revendications précédentes, dans lequel le médicament est sélectionné parmi le groupe composé : (a) d'ibuprofène ; (b) de lysine de déxibuprofène ; (c) d'une combinaison d'ibuprofène et de pseudoéphédrine ; (d) de lopéramide ; (e) d'acétaminophène et d'hypochlorure ou de citrate de diphénhydramine ; (f) d'une combinaison d'acétaminophène, de pseudoéphédrine, de dextrométhorphan et de chlorphéniramine ; ou (g) d'une combinaison d'un analgésique sélectionné parmi le groupe composé d'ibuprofène, d'acétaminophène et d'aspirine avec de la pseudoéphédrine, de la chlorphéniramine ou du dextrométhorphan.

6. Un procédé de préparation d'un comprimé de médicament à mâcher comprenant les étapes consistant à :

enrober les granulés de médicament avec 5 à 28 % en masse, sur la base de la masse sèche des granulés de médicament enrobés, d'un mélange polymère : (a) d'acétate de cellulose, d'acétobutyrate de cellulose ou d'une combinaison de ceux-ci, et (b) d'hydroxypropylcellulose, dans lequel le rapport de masse entre (a) et (b) est compris entre 97:3 et 50:50 ; et

former un comprimé à mâcher en comprimant le médicament enrobé en présence d'excipients.

7. Une méthode selon la Revendication 6, dans laquelle le médicament comprend de l'ibuprofène, de l'aspirine, du naxoprène, de l'acétaminophène, de la lopéramide, de la pseudoéphédrine, du dextrométhorphan, de la chlorphéniramine, de la diphénydramine, de la famotidine, de la cimétidine, de la ranitidine, de la nizatidine, ou des sels ou mélanges de ceux-ci.

8. Une méthode selon la Revendication 6, dans laquelle le médicament est de la lysine de dexibuprofène.